Fifty Thousand Strong: The Sister Study, with Dale Sandler

Ashley Ahearn

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In the United States more than 40,000 women die of breast cancer each year, and almost 200,000 women develop the disease. Although survival rates have improved and risk factors have been identified, the causes of breast cancer remain unclear. In 2004 researchers at the National Institute of Environmental Health Sciences (NIEHS) began recruiting sisters of breast cancer patients for a study to explore environmental and genetic factors behind this disease. Now that more than 50,000 women have been recruited, Dale Sandler discusses what comes next for the Sister Study. Sandler is the principal investigator of the Sister Study and chief of the Epidemiology Branch at the NIEHS.

AHEARN: It's *The Researcher's Perspective*. I'm Ashley Ahearn.

In the U.S. over 40,000 women die of breast cancer each year, and almost 200,000 women develop the disease.[1]

Millions of dollars have been funneled towards researching the causes and treatments of breast cancer. But while survival rates have improved,[2] the causes are still unclear.

The National Institute of Environmental Health Sciences has enrolled 50,000 women in what's called the Sister Study to explore environmental and genetic factors behind breast cancer.

Joining me to talk about it is Dr. Dale Sandler. She's the principal investigator of the Sister Study and chief of the Epidemiology Branch at NIEHS.

Dr. Sandler, thanks for being here.

SANDLER: Thanks for having me.

AHEARN: Tell me about the Sister Study. How is it constructed?

SANDLER: So, the Sister Study is a prospective study of over 50,000 women who have a sister with breast cancer. The study was designed to focus on the role of the environment and genetic factors in breast cancer risk. But because we're focused on women who have a sister with breast cancer, we know that on average they're at twice the risk of developing breast cancer. More of our sisters will have potential variations in their genetic makeup or environmental exposures that may relate to breast cancer both because of the fact that they are related to somebody who had breast cancer and because of the way genes and environment are shared in families.

AHEARN: How much do we know about specific genes and breast cancer?

SANDLER: Well, we're learning more and more. We do know that there are several genes that I'm sure you're familiar with: the breast cancer determining genes *BRCA1* and *BRCA2*, where women who have those genes are at very high risk of developing breast cancer. But in fact only a very small percentage of women with breast cancer have one of those known genes. And so what we're interested in is variations in genes that don't have high predictive value for breast cancer but may play a role in the way your body handles chemicals that it's exposed to; the way it processes hormones.

AHEARN: What kind of environmental factors are you most curious about when you look at gene–environment interactions with breast cancer?

SANDLER: Well, we have clues that hormones are playing an important role in the development of breast cancer. Most of the risk factors that have been clearly established, in addition to family history, relate to your endogenous and exogenous use of hormones—so the use of hormone replacement treatments, women who have higher estrogen levels. And we know that estrogen promotes the growth of breast cancer cells, and so we'll be interested in chemicals in our environment that behave like estrogens or

interfere with the actions of estrogens. There are a lot of things that people are interested in that are sort of common by-products of modern living.

AHEARN: Beyond chemicals, what other factors are you curious about?

SANDLER: We're also interested in lifestyle factors. So, we know that women who exercise regularly have reduced risk for breast cancer, and so we are looking at exercise, but we're looking at it across the life span of the woman. So we're interested in physical activity before or around the time of puberty as well as during the reproductive years and closer to the time of breast cancer risk. We're interested in diet, and we are interested in the role of obesity, which is an important contributor to breast cancer risk and risk for a whole host of other chronic diseases.

AHEARN: You're also a co-investigator of the Two Sister Study. What's that?

SANDLER: Yeah, I'm glad you asked. The Two Sister Study is an offshoot of the Sister Study. One of the things that we had heard was, you know, "Why aren't you studying the women with breast cancer? Why are you studying their sisters who *don't* have breast cancer?" And I've explained about the advantages of our prospective design, but many of the women who joined the Sister Study joined because they had a sister who was diagnosed at an early age with breast cancer. And so with help from funding from the Susan G. Komen Foundation we are able to carry out a family-based study where we are looking at that sister who was diagnosed with breast cancer before the age of 50 and her unaffected sister in the Sister Study, as well as their parents.

We collect genetic material from the parents—we collect spit, in fact, which we can use to look at their DNA—and we can use this to look at risk factors for early-onset breast cancer. And so we will do direct comparisons using the family to look at differences in inheritance of genes from the parents to the sister who got breast cancer early and the sister who didn't; we'll compare the two sisters directly for differences in environmental and lifestyle factors and use this to look at gene–environment interactions in risk for

breast cancer in a different type of a design that in some ways is more sensitive. We're also working with the CDC now to create a cohort of young breast cancer survivors who will come out of this project who we will follow into the future to learn what are the factors that affect quality of life and good survival following the diagnosis at a young age.

AHEARN: As of October of last year 900 of your Sister Study participants, who didn't have breast cancer when they enrolled, had been diagnosed with the disease. I mean, you're dealing with some major emotional factors in conducting scientific research here. Can you talk a little bit about that?

SANDLER: Yes. It's an interesting process to be studying women who join the study because their sister has breast cancer, and they, some of them, joined because they wanted to help their sister or help other women who are at risk for breast cancer. And then as we're following them, some of them do, unfortunately, develop breast cancer, and as I mentioned, about twice as many as you might expect in a general population. So with 50,000 women we think 300 women a year in our cohort will report breast cancer. So every year we contact women to update their health status and it's, it's hard. It's hard for them because some of them have become breast cancer cases, and we are hoping that women will stay with us even after they have developed breast cancer because we think we have a lot to learn about the role of the environment and genes in how well women do after they've been diagnosed with breast cancer.

AHEARN: How do you talk to those women? I would wonder, is there a certain degree of resentment towards your study? I know that's maybe unfounded but just anger associated with this and what's happened to these women?

SANDLER: You know, there's a whole range of responses. Some women join the study, and they understood what we're doing and they understand that they're in the study because they're at risk, and, you know, women everywhere are at risk. There's nobody that's immune, really. Women who develop breast cancer, some of them, we're the

second call—you know, they get the diagnosis, they call their husband, and they report it to our office. We have very amazing participants in our study. Some women join the study thinking joining the study was a magic bullet and they won't get breast cancer if they join the study, or they join the study because they were the "good" sister; they were the one who didn't have breast cancer. But I think women eventually realize that taking part [in] a study is a positive thing that women can do to contribute to the greater good, to contribute potentially to the next generation in their own families, and so the women who join are very committed to helping to finding factors that lead to breast cancer so that someday we'll be able to turn that into prevention strategies.

AHEARN: What are your hopes for the future of the Sister Study?

SANDLER: So, we're following the women over time, and our original scientific goal was to be able to look at the interaction between genetic factors that may make you more susceptible or affect the way you handle chemicals and those true environmental exposures, chemicals in the environment, that have not been as well studied by others as women who are concerned about breast cancer would have hoped. And so our goal will be to carry out sort of these large-scale studies focused on specific genes and chemicals together. We also hope that our study will help us learn about factors that contribute to a good outcome, so we know that the treatment you receive and the stage of diagnosis contribute to how well you do after a breast cancer diagnosis. But we believe that lifestyle and environment factors as well as your genetic makeup may also contribute. So that's sort of a second piece of our study, and because we have a prospective study we're able to look at other things besides breast cancer. More of the women in our study will develop heart disease or osteoporosis or diabetes, in fact, than will develop breast cancer, and so what we have created is this tremendous opportunity to study the role of the environment and genes in conditions that are important to women everywhere.

AHEARN: Dr. Sandler, thanks so much for joining me.

SANDLER: Oh you're welcome. It was my pleasure.

AHEARN: Dr. Dale Sandler is the principal investigator of the Sister Study and chief of the Epidemiology Branch at the National Institute of Environmental Health Sciences.

And that's *The Researcher's Perspective*. I'm Ashley Ahearn. Thanks for downloading![3]

References and Notes

1 U.S. Cancer Statistics Working Group. United States Cancer Statistics: 1999–2006 Incidence and Mortality Web-based Report. Atlanta, GA:Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute; 2010. Available: http://www.cdc.gov/uscs [accessed 17 May 2010].

2 Altekruse SF, et al. (eds). SEER Cancer Statistics Review, 1975–2007. Bethesda, MD:National Cancer Institute (2010). Available: http://seer.cancer.gov/csr/1975_2007/ [accessed 17 May 2010].

3 For more information about the Sister Study and the Two Sister Study, visit http://www.sisterstudy.org/.

Ashley Ahearn, host of *The Researcher's Perspective*, has been a producer and reporter for National Public Radio. She is an Annenberg Fellow at the University of Southern California specializing in science journalism.